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ROUND TABLE

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WHAT PROGRESS IN CANCER RESEARCH?

A Radio Discussion by CHARLES HUGGINS
CARL R. MOORE *and* C. P. RHOADS

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Around the Round Table . . . .

CHARLES B. HUGGINS, professor of surgery at the University of Chicago, was born in Halifax, Canada. After receiving his B.A. degree from Acadia University in 1920, he entered the medical school at Harvard University, where he received his M.D. degree in 1924. Dr. Huggins interned in surgery at the University of Michigan for two years and remained there as instructor in surgery until 1927, when he was asked to join the staff of the University of Chicago. He has been associated with the University in varying capacities since that time, having become professor of surgery in 1936. In 1943 the National Academy of Science granted him the Charles L. Meyer award for his research on cancer.

CARL R. MOORE, professor of zoölogy at the University of Chicago, has been connected with the University since he joined the faculty as an assistant instructor in zoölogy in 1914. Mr. Moore did his undergraduate work at Drury College, where he received his A.B. degree in 1913 and his M.S. degree in 1914. He was granted his Ph.D. degree from the University of Chicago in 1916, and during the summers of 1914, 1915, and 1916 he pursued a course of graduate study at the Marine Biological Laboratory in Massachusetts. During the period from 1911 to 1914, while still attending Drury College, he acted as laboratory instructor there. Mr. Moore has held the professorship in zoölogy at the University of Chicago since 1928. His special interest in the field of cancer research has been directed to those problems which are concerned with the effects of hormones of the organism on the growth processes of the reproductive system and the effects of hormones on the differentiation of the reproductive organs. He is a member of the editorial board of the *Biological Bulletin* and *Physiological Zoölogy*.

C. P. RHOADS, director of the Memorial Hospital for the Treatment of Cancer and Allied Diseases, attended Bowdoin College, where he received his A.B. degree in 1920, and the medical school of Harvard University, where he was graduated *cum laude* in 1924. Dr. Rhoads served as assistant pathologist at the Boston City Hospital from 1926 until 1928, when he became associated with the Rockefeller Institute for Medical Research. In 1933 he was asked to become an associate member of the Institute, in which position he remained until 1939. He has been director of the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York City, since 1940. He is a member of several organizations, among which are the Society of Experimental Pathology, the Association of Pathologists and Bacteriologists, and the Association of American Physicians. He is the author of a number of medical articles which have appeared in professional journals.

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What Progress in Cancer Research?

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MR. MOORE: One hundred and seventy-five thousand Americans die of cancer each year, and fifteen million of our citizens now living will succumb to this painful disease unless something timely is discovered. What is being done to combat the disease? Is there any hope of a cure for cancer? What are the research workers thinking? How do they go about their work? Is the cancer problem being studied by research workers with hopeless pessimism, or is there any indication that progress is being made?

DR. RHOADS: I must differ very sharply with one assumption that you have made. You ask if there is any hope of a cure for cancer. Now this assumes that there are no cures now. The fact is that there are many cures of cancer today, and the number is increasing rapidly. For example, of all the patients treated in good hospitals for early cancer of the breast, 75 per cent are now being cured. This is done simply by the use of the standard surgical procedures which have been developed to the present high degree of perfection. Please notice that I said *early* cancer of the breast. There is still plenty of room for improvement.

DR. HUGGINS: The wonderful advances which have been made in the last century are evidence that great progress has evolved, and confidence is inspired that future important advances will be made. One hundred years ago knowledge of cancer was shrouded by empiricism and mystery. Nearly all the knowledge then available about cancer has turned out to be false. For example, the prevalent idea among surgeons was that cancer was usually incurable. All this has been swept away.

To illustrate the progress of surgery, consider that one hundred years ago there was no anesthesia, and operations were

carried out with no way to relieve the pain. This was changed when ether was introduced, making surgery painless. In addition to being made painless, surgery has become very safe, since bacteria as causes of infection were discovered by Louis Pasteur in the late fifties. Since then, very good ways of controlling infection have been introduced into medicine.

At the present time, Dr. Moore, early cancers may be removed safely from all regions of the body, and a vast number of cures have been brought about.

MR. MOORE: What is cancer, anyway?

DR. HUGGINS: Cancer is a newly formed growth. It can occur anywhere in the body and will spread to other regions and will kill the patient unless medical treatment is carried out.

Present-day methods of treatment are limited when the growth is widespread. Cancer research now has as its immediate goal the treatment of far-advanced tumors. I am sure that the importance of research methods, both in medicine and in industry, is unquestionable. The products of research have profoundly affected the national health and also everyday living. Research indicates dissatisfaction and a desire to do better.

DR. RHOADS: There are two ways of doing the job better. First, we can apply better the knowledge and techniques which now exist; second, we can develop, by research, new and better knowledge and techniques.

As you said, Dr. Huggins, the better use of existing methods depends upon our ability to detect and to treat, in its really early stages, cancer. Early recognition in turn depends, first, upon the education of public and physician and, second, upon provision of facilities for health examinations of apparently well persons at regular intervals.

My first point, public education, means that *everyone* must be trained to go to a qualified physician whenever he or she

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notices any abnormality which may mean the presence of cancer. Delay is a very serious matter. On the average, six months now elapse between the time a patient first notices something is wrong and the time the patient first goes to a doctor. Not only must laymen be better informed, but also doctors must become even more conscious than they now are of the imperative need for immediate treatment of changes which are cancer, or which may develop into cancer. On the average, a second period of six months elapses between the time the patient first goes to a doctor and the time when effective measures of cure are instituted. This total delay of a year often means time for the growth of the cancer from an early, curable state to an incurable state.

My second way of improvement is the provision of clinics for examining apparently well individuals for the presence of cancer or for changes which may become cancer.

MR. MOORE: What can we do about this?

DR. RHOADS: Well-person cancer prevention clinics of this type, like the Strang Clinic in New York, are now springing up all over the country. Many cancers begin so insidiously that the patient is not aware of and cannot detect any change at all. Regular examination by physicians is required to reveal these early, silent cancers. Once discovered, however, they can be cured with comparative ease.

MR. MOORE: As a means of giving some adequate conception to our listening audience of the general nature of cancer, would it be fair to say that in the beginning cancer is merely an unusual activity in the multiplication of cells which may occur in any part of the body?

For example, a pinpoint area of cells in the skin might begin to grow. The cells are not dead; they are merely multiplying, and multiplying too rapidly. They are producing more cells of a type that do not respond to controlling forces as do other healthy cells of the body. The growth in the beginning is not large; it is not painful; and if the cells would only stop multiplying, all would be well.

Many people ask, Dr. Huggins, if cancer is contagious.

Dr. Huggins: Cancer is certainly not contagious. Although it may be inoculated from animal to animal, there is absolutely no danger of a person with cancer transmitting it to his family or his associates.

Mr. Moore: What do you think about the inheritance of cancer, Dr. Rhoads?

Dr. Rhoads: Animals can be bred in strains so pure that every single individual of many successive generations will develop cancer. Very fortunately, the breeding of human beings is not quite so rigidly controlled, and we do not have any pure strains. Without many generations of inbreeding, it is almost impossible to prove the existence of an inherited trait, so we have no sure evidence that cancer is hereditary in man.

There is no absolute proof that a person whose parents had cancer is more likely to develop the disease than is an individual who has no cancer in his family. We do sometimes strike rare examples where the same type of cancer has occurred in several generations, but there are so many exceptions that I could not draw a general rule.

Mr. Moore: So these cancer cells simply continue to grow and get more and more out of control and invade other tissues next to them. Do they ever invade the blood stream and go to other organs?

Dr. Huggins: They certainly do. They spread in several ways, and it is with this type of widespread and advancing lesion that the research worker is mostly concerned, since under these circumstances the surgeon has no capacity to remove the lesion. In dealing with advanced cancer, however, other methods of treatment are available. The use of radium and X-ray has given extremely valuable results in your clinic, has it not, Dr. Rhoads?

Dr. Rhoads: Certainly—in all clinics! It is very useful in curing some types of cancer in areas which cannot be removed surgically without serious deformity or serious interference with normal body function.

Dr. Huggins: Are there limitations to the use of these meth-

ods, such as occur with surgery, or are radium and X-ray the best techniques we can hope for in cancer treatment?

DR. RHOADS: The methods of using radium and X-ray are being constantly improved. In the cure of cancer they will always be limited in their application to cases in which the cancer is discovered early, while it is still confined to the area in which it arose.

MR. MOORE: This may apply all right to local cancers, but is there any help for the more extensive growths?

DR. RHOADS: It seems to me that recent discoveries provide very great hope for the future. For example, certain cancers of sex organs now can be controlled, temporarily, without any surgery at all. This is done by the use of chemicals which have the power of restraining the growth of these organs and of the contained cancer as well.

Another exciting development is that chemicals have recently been found which have the power of destroying certain types of body cells without any damage to the rest of the body. By the use of these chemicals we can also destroy, temporarily, cancer of similar cell types.

Now we are all looking for more effective chemicals. There is new knowledge coming along all the time. Many scientists are now working on the problem of cancer and on growth as a whole. They will certainly find new methods which will allow more adequate control of cancer by nonsurgical means. This may sound overoptimistic, but we will certainly find no new cure if we do not look for one.

MR. MOORE: I wonder if this does not bring us back to the general principle of the need for more fundamental knowledge of cell growth. It has often seemed to me unnecessary to think of cancer as a sickness of only the human body. We can investigate the problem, can we not, by using many different types of animals lower than man, in which a study can be made of the forces which control growth activity, which make cells multiply, or which may prevent their multiplication? And is it not true that we can study these problems on such living things as mice

or chickens, or even plants? I know of some work, for example, where certain chemicals have been applied to the stem of a tomato plant, which caused the cells to multiply and grow into large tumor-like masses.

Dr. Rhoads: Certainly, we must consider and study the whole organism, be it tomato plant or man, not merely the cancer alone. We have to learn all about the chemical disorders present in the body in which the cancer is growing, since some fundamental abnormality must exist which causes this cancer and allows it to keep on growing.

Second, I feel sure that we must make detailed, precise studies of cancer cells in comparison with normal cells of the same types. We have to study the composition of these cells as well as their function. If we can only find an abnormal constituent or characteristic of a cancer cell, perhaps we can use the finding to great advantage.

For example, the cancer cell might be found to depend for its structure on something which is not present in the normal cell. If this were the case, we conceivably could develop chemical compounds which would destroy this special substance in the cancer cell, and thereby destroy the cell itself without injury to the normal cells lacking this special substance.

Mr. Moore: Do human individuals have any natural defense against the spread of cancer?

Dr. Huggins: Yes, indeed! Some people develop a cancer which will remain dormant for many years, say ten years or more; whereas other patients with the same type of growth have a fatal outcome from the cancer in ten weeks. This is why we must know more of the chemistry of cancer.

Mr. Moore: A statement is often made that cancer is on the increase. Is this true or false?

Dr. Rhoads: It is entirely true that the number of deaths from cancer in the country annually is on the increase, but this is due to the fact that each year the average age of the population is older. If one adjusts the death rates for the age of the population, deaths from cancer are decreasing, as proved by recent statistics.

MR. MOORE: Are there any known factors or predisposing conditions which frequently lead to cancer or which give us a means of understanding the origin and development of the disease?

DR. RHOADS: Let me quote you a very interesting example. I know an old British soldier. He told me a few months ago that for a few weeks he noticed on the side of his tongue a firm, white, slightly elevated patch, about the size of a pea. This stood out in sharp contrast to the normal red, rough surface of the tongue.

One day he looked in his mirror and saw the area had changed. It had become an ulcer, shiny, gray-white, with a firm white edge; and when he scratched it, it bled. This original white patch was composed of abnormal cells which had not quite become cancer cells. The ulcer, at the later stage, was made up of invading cancer cells. Now, either type of cell can be scraped off, put in the test tube, and studied.

MR. MOORE: What should he have done about it, if anything?

DR. RHOADS: He should have gone promptly to his doctor and had the white patch removed. He was afraid to do so. He allowed the change to progress until the abnormal cells which made up the white patch had become malignant, had become able to grow more rapidly, able to replace the normal tissue of the surface of the tongue, and able to destroy the body if not treated in time. At this stage he sought medical attention. The ulcer was removed surgically, and he will be cured.

MR. MOORE: What factors would you say play a role in producing such a growth on a man's tongue?

DR. HUGGINS: There are three or four factors which may be involved in the formation of this particular growth. The patient was a male, and cancer of the tongue occurs much more frequently in males than it does in females; this implies a sex linkage of some sort. This sex linkage may be a clue for research because sex changes are controlled by certain compounds which can be studied in the laboratory.

DR. RHOADS: That is a very interesting matter. There is a

strong tendency for cancer of the tongue and mouth in general to occur in men.

This individual (my British soldier) also illustrates the fact that cancer tends to occur after the fortieth year. Furthermore, he smoked heavily, and he had a rough tooth, which often scratched his tongue. There is no proof that smoking causes cancer at all, and I do not believe it does; but there is reason to believe that if the tissue surface is likely to develop cancer, chronic irritation of any kind, as from a rough tooth, may well accelerate the process.

MR. MOORE: If we are going to tackle these problems in an experimental laboratory, we need a means of approaching the problem other than trying to produce abnormal lesions in the human individual. I do not believe any of us would willingly submit to experimentation upon ourselves with the hope of inducing a cancerous growth.

DR. HUGGINS: Fortunately, within the last forty years, remarkable advances have been made in research in laboratories; this has been true largely because of the introduction of methods of producing cancers in animals.

MR. MOORE: How great is the importance of the use of experimental animals in these studies?

DR. HUGGINS: The experimental animals are highly important in cancer research. In fact, they are the basis of research work in modern cancer laboratories; and any interference with the use of animals in laboratories is an opposing force to research in cancer.

By the use of animals, great advances have been made in studying heredity and the factors necessary to the formation of cancer. We have learned how to produce cancer in mice and have made a beginning in chemical methods of treatment. Research on animals is still proceeding, and many more advances can be confidently predicted.

MR. MOORE: I gather from those statements that you would regard any proposal to make it impossible to use animals in research on cancer as an obstacle in the path of obtaining a solution to the problem of cancer.

Dr. Huggins: There is no doubt that such a decision would slow up the study of cancer and the development of new methods for diagnosis and treatment very seriously—actually more than any other factor which I can imagine.

Dr. Rhoads: In this connection I can give a very good example. It is possible to breed strains of mice so pure that essentially every individual will, at about the same period of life, develop the same type of cancer.

You can see what this means. It means that we can have a constant supply of animals with cancer or of cancer cells to compare with normal animals, or normal cells of the same type. We can test chemical compounds on these mice to restrain the growth of the cancer cells, or we can remove the cells and grow them in tiny glass vessels parallel with normal cells, to ascertain the points of similarity and the points of difference. Indeed, it is now possible to grow these cancer cells on the developing chick embryo in the hen's egg, and so be able to test compounds on the cells.

Mr. Moore: Someone suggested that we may be able to utilize many of the new discoveries which have come from work on the atomic bomb. Do you see any application of such new information, or of such substances as may have been obtained from studies on atomic energy, to this problem of research in cancer?

Dr. Huggins: The development of knowledge incident to atomic research, which culminated in the atomic bomb, has been very great. It has been the usual experience in science that a great discovery in one field is likely to cause reverberations and advances in many neighboring fields of scientific activity, and so it is in this one.

Atomic research has provided us with a great variety of new radioactive compounds which are of importance in research, as well as in treatment. To cite one important example, we now have radioactive iodine which is able to affect, beneficially, growths of the thyroid gland. However, the great immediate importance of atomic energy to medicine is in providing us with compounds for laboratory investigation. These newly available

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chemical compounds are tracer substances with labels attached, so to speak, which will provide valuable knowledge about the functioning of the cell. It is certain that new methods of treatment will evolve from the use of atomic products in laboratory investigations.

Mr. Moore: What do we know of the effects on man from exposure to the radioactive forces generated by such an explosion as the atomic bomb? Has any work been done on this?

Dr. Rhoads: A commission has just been established by the National Research Council to study this very point. As far as we know now, one could expect from the energy of the atomic bomb exactly the changes which occurred in the early students of X-ray and radium who were not aware of the hazards of atomic energy. Almost all of these individuals died of cancer of the tissues which had been exposed directly. There is very good reason to believe that cancer can be produced by energy of the type developed by the atomic bomb.

Mr. Moore: To return to the matter of the chemical treatment of cancer, I should like to mention the further studies of those substances in the body which we call hormones. The sex glands, especially, secrete hormonal substances, which stimulate growth in certain of the organs which make up the reproductive system. These are, in the first case, normal processes. The normal functioning of the various organs is necessary to insure the reproduction of the race.

The function of the mammary glands or breast tissue of woman is under the control of hormones. The development of such an organ in the male as the prostate gland is under the control of hormones. It is necessary to have these hormones present for the normal functioning of many of the organs of reproduction. This means not only the function of the cell but actually the growth of new cells.

Some strains of mice exist in which a large percentage of females die of breast cancer, but the males do not have cancer, largely because of too little actual breast tissue. But if we treat the male with female hormones, the males will develop breast cancer. Some organs in the males can be increased ten times by

treatments of male hormones. This great increase in the multiplication of cells, however, is not cancer, but it may aid in the development of cancer.

On the other hand, the removal of hormones from the body, or their inactivation, may, in some cases, slow up cancer activity. How important the hormones are in causing cancer is a very live question at the present time.

This brings us to a province where Dr. Huggins has made some recent phenomenal advances. Tell us about the work on cancer of the prostate which you have been investigating for a number of years, Dr. Huggins.

DR. HUGGINS: I blush as much as anyone can on the air over your use of the adjective "phenomenal," but it has developed that some of the tissues acted upon by hormones, when in a cancerous condition, recede, provided adequate chemical treatment is given. While the results have been so far restricted, an advance has been made in the fields of cancer of the breast and cancer of the prostate.

MR. MOORE: Is this all surgery, or is some of it just ordinary medical treatments?

DR. HUGGINS: The basic treatment may be conceived to be a chemical treatment, since the administration of hormones sometimes causes widespread cancer to recede. This is of some theoretical interest, since it is an example of profound regression of widespread cancer by medical methods which bring about shrinkage of cancer not possible in any other way.

The surgeons continually attempt to convert formidable surgical procedures into smaller ones and even to go further by converting surgical treatment into medical treatment.

MR. MOORE: We have talked of some of the progress which is being made in cancer research. We are cheered by the progress which has been made and we are hopeful about future progress. What can be done to secure the greatest success in cancer research?

DR. HUGGINS: The National Science Foundation Bill, which is intended to aid research on many scientific projects, is con-

cerned with provision by the government of large sums of money for scientific research.

However, I should point out that the scientists are less concerned with how the funds become available than with having sufficient resources to tackle this serious problem of cancer adequately. They have a citizen's interest, of course, in the raising of funds, but how the funds are provided is a political and social problem in which research workers do not have special competence. This National Science Foundation Bill would affect profoundly cancer research.

MR. MOORE: In addition, there is the Neely-Pepper Bill, which would provide for the expenditure of one hundred million dollars on research in cancer.

The experience of the atomic bomb, in which billions of dollars were spent and thousands of scientists assembled on a common problem, would, because of its success, naturally raise the question of whether a similar program should not be undertaken in cancer. After all, more people died in the United States of cancer during the war than the nation lost in killed or missing in action during the war.

DR. RHOADS: The primary need is for research on an inclusive scale, developed around the scientists in the university laboratories. The problem of cancer is an extraordinarily broad one. It involves practically every problem in biology. It must be studied by the techniques and concepts of physicists, chemists, botanists —indeed, of every basic science. It is a mistake to assume that we can say precisely what approach we should take. We cannot exclude any proper approach. We must study every detail of cell function, composition, and growth. Every path which gives promise must be pursued.

There are two methods of making advances in science. One is the support of all kinds of fundamental research likely to provide us with new information and techniques. The second is the creation of special institutes in which all types of apparently useful techniques in the hands of those competent in using them may be brought together to bear directly upon the cancer problem. Neither method is likely to be effective alone, but with both

the broad support of fundamental research and the ability to develop this research into the cancer problem, progress is likely.

DR. HUGGINS: The idea of a cancer institute is a sound one for cancer research. I might define an institute as a collection of scientists of various disciplines in a situation where they can work together, talk, and cooperate.

I think that this method of procedure is preferable to widely diversified individuals working in scattered regions of the country. The Memorial Cancer Center is a good example of what I mean by a cancer institute.

DR. RHOADS: I believe completely in the institute principle with one qualification: We must remember that the source of the essential trained personnel is the universities. It is expensive and difficult to create a highly trained research person. People do not realize the kind of process it is, and how hard it is to train research people in large numbers. There is desperate need for the scientifically trained men and women who will be able to make the new discoveries which will lead to a cure for cancer.

These men and women must be trained in the universities. The facilities and funds for the training must be provided. Talented young people must be sought out, led in the research work, and given the chance to work productively and in comfort.

The administration of funds in support of cancer research cannot be done as an avocation, like playing golf on week ends. It requires constant thought about the cancer problem, broad familiarity with biological science as a whole, an unerring judgment regarding scientific personnel, and close contact with the scientist. Finally, there must be the courage to back the desperate venture and to organize and carry through extensive projects.

Such administrators are not found overnight. They must be selected, trained to work as a group, and, finally, given authority to do their job without interference.

MR. MOORE: Today's discussion of cancer research has shown us, in general, to be somewhat optimistic. We have emphasized the paramount importance of early recognition of unusual growth processes. Surgery, and in some cases radiation, are effec-

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tive cures. One of the hoped-for goals is to learn of some further means of treatment which will prevent or stop local cell multiplication by the application of chemicals or radiation.

The cancer problem is exceedingly broad and complex, and until we develop still more adequate treatments than we now have, adequate funds must be made available for research. There is no doubt that further research gives the promise that man may be able ultimately to control this devastating disease, as he has been able to do in the case of so many other serious diseases.

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